REMARKS

Reconsideration and reexamination of the present application are respectfully requested in light of the foregoing amendments and the following remarks.

1. Status of the Claims

The status of the claims following entry of the amendment is as follows:

Claims canceled: Claims 1-5, 8-22, and 28

Claims pending: Claims 6-7, 23-27, and 29-30

Claims previously allowed: Claims 6, 25-27, and 29

Claims rejected: Claims 6-7, 23-27, and 29-30

Claims withdrawn: Claim 23

2. Request for Consideration of Information Disclosure Statement

Applicants request consideration of the IDS filed September 9, 2008, in the next communication from the Office.

3. Request for Rejoinder

Claim 23 remains withdrawn as directed to non-elected subject matter, following a restriction requirement mailed Dec. 16, 2005. Because claim 23 is a method of using the polypeptide fragment of allowed claim 25, Applicants respectfully request rejoinder and examination of claim 23 pursuant to the Office's rejoinder policy stated in MPEP § 821.04(b).

4. Priority and Certified Translation of JP 2002-2056

The Office considers the effective date of the invention to be February 15, 2005, the filing date of the present application. The Office requires an English translation of the priority document, JP 2002-2056, filed January 9, 2002, to accord it the benefit of priority. Applicants submit herewith a certified translation of JP 2002-2056. Accordingly, the effective date of the invention is January 9, 2002.

5. Rejection under 35 U.S.C. § 101

Claims 25 and dependent claims 6-7, 24, 26-27, and 29-30 are rejected under 35 U.S.C. § 101 as allegedly directed to non-statutory subject matter. The Office alleges that the claimed polypeptide fragments occur in nature.

Applicants traverse the rejection. Solely to expedite prosecution, however, Applicants follow the Examiner's suggestion to amend claim 25 to clarify that the claimed polypeptide fragment is isolated. Claim 30 is likewise amended.

6. Rejection under 35 U.S.C. § 112, First Paragraph (Enablement)

Claim 25 and dependent claims 6-7, 24, and 26-27 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled by the specification.

Applicants traverse the rejection. Enablement is determined by an analysis of the *Wands* factors. *In re Wands*, 858 F.2d 731, 736, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988). The *Wands* factors include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In the present case, the Office bases the rejection on a mischaracterization of the claims. With respect to the breadth of the claims, the Office alleges that the claimed polypeptide "comprises any basic amino cluster region having neovascularization activity." This is incorrect. Claim 25 recites in part that the polypeptide fragment of an N-acetylglucosaminyltransferase V (GnT-V) may comprise a basic amino acid cluster region that is a variant of the basic amino acid cluster region comprising the amino acid sequence of SEQ ID NO: 7 and up to 50 contiguous amino acids encoded by the sequence shown in SEQ ID NO: 6, wherein the variant possesses neovascularization activity, wherein the number of amino acids modified by addition, removal, or substitution in the variant is up to 10% of the number of amino acids in the basic amino acid cluster region, and wherein the addition, removal, or substitution is conducted on amino acids other than basic amino acids.

The Office cites the Whisstock reference for the proposition that this art is generally unpredictable. The Office further alleges that Applicants provide no guidance as to which regions of the protein may be modified without affecting activity, the general tolerance of the protein to modification, a rationale for how to modify amino acids, and guidance as to which choices of amino acids to modify would be successful.

To the contrary, Applicants' specification provides sufficient direction or guidance and working examples to comply with the enablement requirement. Because the addition, removal, or substitution is conducted on amino acids other than basic amino acids, all the claimed polypeptide fragments comprise a basic amino acid cluster region having the amino acid sequence of SEQ ID NO: 11, which is part of SEQ ID NO: 7. Applicants demonstrate that SEQ ID NO: 11, KRKRKK, is ***sufficient*** for the polypeptide fragment to possess neovascularization activity. *See, e.g.*, Specification, page 45, lines 22-27 ("the KRKRKK peptide accelerated growth of HUVEC at the same degree as GnT-VΔ73. . . . These results suggest that a basic amino acid cluster region of GnT-V is sufficient for an HUVEC growth accelerating activity. . . ."); *see also* Specification, pages 46-48, FIGURES 3, 4, 5, and 6, etc. The Specification provides further evidence that polypeptide fragments of SEQ ID NO: 6 that comprise SEQ ID NO: 11 possess neovascularization activity: Gnt-VΔ73 (page 41, line 27, *et seq.*; page 46, lines 3 – 21); Gnt-VΔ188 (page 42, lines 22 – 24, *et seq.*; page 46, line 23 – page 47, line 6); and Gnt-VΔ233 (page 42, line 24 – page 43, line 1, *et seq.*; page 46, line 23 – page 47, line 6).

The Office provides no evidence that members of the genus would not have the stated activity. Further, the Office advances no evidence that merely adding, deleting, or substituting amino acids to a polypeptide would require more than the exercise of routine skill. The enabling disclosure instead in commensurate with the scope of the claims, because all the recited polypeptides comprise SEQ ID NO: 7, which is sufficient for neovascularization activity. The specification establishes which regions of the claimed polypeptides may be modified without losing neovascularization activity (i.e., thus outside the region KRKRKK), and provides sufficient guidance and direction to the skilled artisan to make polypeptide fragments and variants thereof that possess neovascularization activity. The presently claimed polypeptide

fragments thus would not require undue experimentation to make and use, and the rejection should be withdrawn.

This rejection is not substantially different from that raised in the Office Action mailed April 11, 2007. This rejection was withdrawn in the Office Action mailed July 11, 2008, following Applicants' Amendment and Response under 37 C.F.R. § 1.114, filed October 31, 2007. To expedite prosecution and avoid repetitive prosecution, examiners are required to give the previous examiner full faith and credit. *See* MPEP § 706.04. MPEP § 706.04 particularly prohibits the rejection of previously allowed claims for any reason other than the citation of a new reference. Independent claim 25 was among those claims previously indicated as allowed. The Examiner is bound by the MPEP. *See* MPEP, Forward. The rejection therefore is improper and must be withdrawn. This response constitutes Applicants' request for reconsideration, pursuant to 37 C.F.R. §§ 1.181 and/or 1.182.

7. Rejection under 35 U.S.C. § 112, First Paragraph (Written Description)

Claim 25 and claims 6-7, 24, and 26-27 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly not adequately described by the specification.

Applicants traverse the rejection. It is by now well established that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . *i.e.*, complete or partial structure, other physical and/or chemical properties, ***functional characteristics when coupled with a known or disclosed correlation between function and structure***, or some combination of such characteristics.' *Enzo Biochem Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 63 U.S.P.Q.2d 1609, 1615 (Fed. Cir. 2002) (citing with approval Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, 66 Fed. Reg. 1099 (Jan. 5, 2001), Example 9 at 35-37; emphasis in original).

The Office alleges that "no additional information correlating structure with function has been provided [in the specification]." Office Action, p. 11. This is incorrect. The scope of the presently claimed polypeptide variants is set forth above. All variants comprise the basic amino acid cluster region having the amino acid sequence of SEQ ID NO: 11, which provides sufficient structure for the claimed polypeptides to possess neovascularization activity. *See, e.g.*,

Specification, page 44, line 15, *et seq.* Further, GnT-V fragments comprising SEQ ID NO: 11 also possess neovascularization activity, including Gnt-VΔ73 (page 41, line 27, *et seq.*; page 46, lines 3 – 21); Gnt-VΔ188 (page 42, lines 22 – 24, *et seq.*; page 46, line 23 – page 47, line 6); and Gnt-VΔ233 (page 42, line 24 – page 43, line 1, *et seq.*; page 46, line 23 – page 47, line 6).

All the polypeptide fragments encompassed by the claims comprise the amino acid sequence of SEQ ID NO: 7, which encompasses SEQ ID NO: 11. Because the peptide of SEQ ID NO: 11 possess neovascularization activity, ***all*** the polypeptide fragments encompassed by the claims likewise would be expected to possess neovascularization activity. This is also clear from the language of claim 25, which recites: "wherein the addition, removal, or substitution is conducted on amino acids ***other than*** basic amino acids." The claims are adequately described, because the Specification describes functional characteristics of the claimed compounds, coupled with a disclosed correlation between function and structure. *See Enzo*, 63 U.S.P.Q.2d at 1618.

The Office cites references by Witkowski and Wishart for the proposition that homologous proteins do not necessarily share the same function. Written description, however, must be determined from the standpoint of the claimed invention. Applicants' specification demonstrates functional characteristics of the claimed compounds, coupled with a disclosed correlation between function and structure, in compliance with the written description requirement for biological molecules. Applicants need not provide more, simply because the art may be unpredictable.

This rejection is not substantially different from that raised in the Office Action mailed April 11, 2007. This rejection was withdrawn in the Office Action mailed July 11, 2008, following Applicants' Amendment and Response under 37 C.F.R. § 1.114, filed October 31, 2007. To expedite prosecution and avoid repetitive prosecution, examiners are required to give the previous examiner full faith and credit. *See* MPEP § 706.04. MPEP § 706.04 particularly prohibits the rejection of previously allowed claims for any reason other than the citation of a new reference. Independent claim 25 was among those claims previously indicated as allowed. The Examiner is bound by the MPEP. *See* MPEP, Forward. The rejection therefore is improper and must be withdrawn. This response constitutes Applicants' request for reconsideration, pursuant to 37 C.F.R. §§ 1.181 and/or 1.182.

8. Rejection under 35 U.S.C. § 102(b)

Claim 25 and dependent claims 6-7, 24, and 26-27 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Taniguchi *et al.*, *Glycoconjugate J.* 18(11-12): 859-65 ("Taniguchi").

Applicants traverse the rejection. Taniguchi is unavailable as prior art under 35 U.S.C. §§ 102(a) or 102(b). As noted above, the priority date of the present application is January 9, 2002, the filing date of JP 2002-2056. A publication disseminated by mail is not prior art until it is received by at least one member of the public. Thus, a magazine or technical journal is effective as of its date of publication (date when first person receives it) not the date it was mailed or sent to the publisher. *In re Schlittler*, 234 F.2d 882, 110 U.S.P.Q. 304 (C.C.P.A. 1956).

Taniguchi shows at the top of the first page a publication date of 2001. Taniguchi, however, was not published in 2001. First, the copyright date of Taniguchi is 2003, not 2001. Taniguchi, header, p. 859. Second, Taniguchi was not received for review until June 17, 2002, and it was not accepted for publication until September 25, 2002. Taniguchi, footer, p. 865. Third, Taniguchi cites two publications, references 50 and 51, which were not published until 2002. Taniguchi, bibliography. Accordingly, Taniguchi could not have been published earlier than September 25, 2002. This date, however, is antedated by the present priority date of January 9, 2002. It follows that Taniguchi is not prior art. *See* 35 U.S.C. §§ 102(a), 102(b). The rejection accordingly must be withdrawn.

CONCLUSION

The application is again in condition for allowance. Acknowledgement of the same is requested. Should the Examiner have any questions or comments regarding Applicants' amendments or response, the Examiner is asked to contact Applicants' undersigned representative at the telephone number below. Please direct all correspondence to the below-listed address. If there are any other fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0573. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is respectfully requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Date: August 7, 2009

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